REMARKS

Claims 1-11 are pending in this application. Claims 1, 2, 4, 8 and 10 have been amended.

Applicants, by canceling or amending any claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants reserve the right to reassert any of the claims canceled herein or the original claim scope of any claim amended herein, in a continuing application.

Independent claim 1 has been amended to recite, "A pharmaceutical suspension formulation comprising a. particles of formoterol or a pharmaceutically acceptable salt thereof, said particles being suspended in the formulation, b. particles of ciclesonide or a pharmaceutically acceptable salt thereof, said particles being suspended in the formulation and a propellant selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane and a mixture thereof." Support for claim 1, as amended, can be found throughout the specification and claims as originally filed. Claims 2-11 depend, either directly or indirectly, from claim 1.

No new matter has been added.

In view of the remarks set forth below, further and favorable consideration is respectfully requested.

I. At page 2 of the Official Action, claims 2, 4, 8 and 10 have been objected to as containing informalities

The Examiner requests that claims 2, 4, 8 and 10 be amended to recite the phrase "further comprising" or "further," after the word "optionally" in claim 2, before "a surfactant" in claim 4, before "comprises" in claim 8 and before "comprising" in claim 10.

In view of the following, this objection is respectfully traversed.

Applicants respectfully submit that claims 2, 8 and 10 have been amended as requested by the Examiner. However, with regard to claim 4, Applicants submit that "further comprising" language is not necessary because the parent claim utilizes open comprising language. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw these objections.

II. At page 3 of the Official Action, claims 1-11 have been rejected under 35 USC § 112, first paragraph

The Examiner asserts that claims 1-11 fail to comply with the written description requirement because the present specification does not disclose how to make solvates of formoterol or ciclesonide.

In view of the following, the rejection of claims 1-11 is respectfully traversed.

Applicants note that claim language directed to "solvates" has been removed from claims 1, 2 and 4. Claims 3 and 5-11 depend, either directly or indirectly, from claim 1.

Applicants note that the amendments to claims 1, 2 and 4 have been made solely to expedite allowance of the present claims. In this regard, Applicants maintain that the present application describes solvates of ciclesonide and formoterol. Therefore, Applicants expressly reserve the right to reassert the scope of claims 1, 2 and 4 in a continuing application.

In view of the foregoing, it is submitted that claims 1-11 fully comply with the written description requirement of 35 U.S.C. § 112, first paragraph. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

III. At page 5 of the Official Action, claims 1-11 have been rejected under 35 USC § 112, first paragraph

The Examiner asserts that claims 1-11 do not provide enablement for compositions comprising any solvates, any hydrates, or other physiologically acceptable derivatives of ciclesonide and/or formoterol, with the exception of formoterol fumarate dehydrate and the 21-hydroxy ciclesonide compound described in the presently claimed subject matter.

In view of the following, the rejection of claims 1-11 is respectfully traversed.

As previously discussed above, Applicants note that claim language directed to "solvates" has been removed from claims 1, 2 and 4. Claims 3 and 5-11 depend, either directly or indirectly, from claim 1. Furthermore, Applicants note that claims 1, 2 and 4 have been further amended to remove claim language directed to "physiologically functional derivatives."

As previously stated, Applicants note that the amendments to claims 1, 2 and 4 have been made solely to expedite allowance of the present claims. In this regard, Applicants maintain that the present application is enabling with regard to describing solvates and/or physiologically functional derivatives of ciclesonide and formoterol. Therefore, Applicants expressly reserve the right to reassert the scope of claims 1, 2 and 4 in a continuing application.

In view of the foregoing, it is submitted that claims 1-11 fully comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

IV. At page 9 of the Official Action, claims 1, 3-6, 9 and 11 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Aberg et al. (US Patent No. 5,795,564) in view of Burt (US Publication No. 2002/0030068), Garcia-Marcos et al. and Calatayud et al. (US Patent No. 5,482,934)

Claims 1, 3-6, 9 and 11 have been rejected under 35 USC § 103(a) as being unpatentable over Aberg et al. in view of Burt, Garcia-Marcos et al. ("Inhaled corticosteroids plus long-acting beta2-agonists as combined therapy in asthma," *Expert Opin. Pharmacother.*, April 2003, 4(1), pp 23-29) ("Garcia") and Calatayud et al. Applicants note that claims 2, 7-8 and 10 were not included in this rejection.

In view of the following, this rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court held in *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 (2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *See KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 at 417-418. Second, the proposed modification of the prior art must have had a reasonable expectation of

success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

Applicants submit that a proper case of *prima facie* obviousness has not been established because whether taken alone, or in combination, none of Aberg et al., Burt, Garcia and/or Calatayud et al. provide sufficient motivation to arrive at the presently claimed subject matter with a reasonable expectation of success.

The Official Action states at pages 10-12:

> Aberg exemplifies a metered dose inhaler containing a suspension formulation comprising R,R-formoterol fumarate dehydrate. Furthermore, Aberg lacks the teaching of compositions comprising formoterol in combination with ciclesonide. Additionally, Aberg lacks the teaching of suspension aerosol formulations.
>
> Burt teaches that suitable alternative propellants include HFA-134a (1,1,1,2-tetrafluoroethane) and HFA-227 (1,1,1,2,3,3,3-heptafluoropropane). Burt identifies several active agents that may be formulated into pharmaceutical compositions in the form of... a suspension... such as anti-inflammatories (e.g. budenoside) and bronchodilators (e.g. formoterol).
>
> Garcia teaches that data for the combination of a long-acting beta-2 agonist (e.g. formoterol or salmeterol) with an inhaled corticosteroid (ICS) in the same inhaler is as effective as administration of a much higher dosage of the ICS alone for the control of asthma.
>
> Calatayud teaches the syntheses, purification, and isolation of ciclesonide and that ciclesonide is desirable for the treatment of inflammatory conditions, because it has a greater therapeutic index than other commonly administered anti-inflammatory steroids (e.g. budenoside, etc.)
>
> It would have been prima facie obvious to combine the teachings of Aberg and Garcia, Burt, and Calatayud, because Aberg teaches that (R,R)-formoterol may be combined with other therapeutic agents. An ordinary skilled artisan would have been motivated to combine the teachings of the cited references, because these references all describe formulations for the treatment of inflammatory diseases (e.g. asthma).

Amended independent claim 1 recites "A pharmaceutical suspension formulation comprising a. particles of formoterol or a pharmaceutically acceptable salt thereof, said particles being suspended in the formulation, b. particles of ciclesonide or a pharmaceutically acceptable salt thereof, said particles being suspended in the formulation and a propellant selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane and a mixture thereof."

Conversely, Aberg et al discloses a metered dose inhaler containing a suspension formulation comprising only R,R-formoterol fumarate dehydrate. As such, Aberg et al. is absolutely silent regarding the presently claimed formulation comprising particles of formoterol and ciclesonide as described in the present subject matter. Aberg et al. does not even discuss ciclesonide, much less the synergistic benefits of a suspension comprising formoterol and ciclesonide. Thus, Aberg et al. do not contemplate the combination of formoterol and ciclesonide in a pharmaceutical suspension.

Therefore, Aberg et al. do not "teach or suggest all the limitations of the claims" as required by *In re Wilson*. The Burt et al. reference does not remedy the deficiencies of Aberg et al. Burt et al. merely describes suitable alternative propellants include HFA-134a (1,1,1,2-tetrafluoroethane) and HFA-227 (1,1,1,2,3,3,3-heptafluoropropane) which may be combined with a combination of formoterol and an inhaled corticosteroid. As such, Burt et al. does not discuss or contemplate a pharmaceutical suspension formulation of formoterol and ciclesonide as recited in the presently pending claims.

The Garcia reference does not remedy the deficiencies of the Aberg et al. and Burt et al. references. Garcia discusses the combination of formoterol and

budenoside. More specifically, the Examiner indicates that Garcia "teaches that the formoterol/budesonide combination was found to improve lung function and asthma control when combined with both low and high doses of budenoside in comparison to asthmatics administered only budenoside." Thus, Garcia does not teach a pharmaceutical suspension formulation of formoterol and ciclesonide as recited in the presently pending claims.

The Calatayud et al. reference does not remedy the deficiencies of the aforementioned references since it does not discuss anywhere the use of formoterol in conjunction with ciclesonide. Indeed, Calatayud et al. provides no indication in any way that ciclesonide can be combined with an additional treatment such as formoterol.

Therefore, there is absolutely no motivation to combine the teachings of the aforementioned references with the teachings of Aberg et al.

Therefore, whether taken alone or together, none of the cited documents teach or suggest a pharmaceutical suspension formulation comprising a combination of formoterol and ciclesonide as required by Applicants' pending claims. As such, Applicants respectfully request that the Examiner reconsider and withdraw this rejection against the presently pending claims.

V. At page 14 of the Official Action, claims 2 and 7-8 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Aberg et al. in view of Burt, Garcia-Marcos et al. and Calatayud et al., and further in view of Fassberg et al. (US Patent No. 5,474,759)

The Examiner asserts that Fassberg et al. teaches pharmaceutical aerosol formulations comprising a medicament, a surfactant, an excipient and a propellant.

In view of the following, this rejection is respectfully traversed.

A brief outline of relevant authority is set forth above in Section IV. Also, all

references other than the Fassberg et al. reference are discussed in detail in Section IV. For the sake of brevity, the discussion of the relevant authority and all references other than the Fassberg et al. reference are incorporated herein in their entirety.

The Examiner relies on Fassberg et al. for its alleged disclosure of surfactants and excipients.

However, the rejected claims are free of the prior art for the reasons discussed above (see, Section IV) and Applicants' arguments stated above are incorporated herein by reference in their entirety.

Accordingly, Applicants respectfully submit that a *prima facie* case of obviousness has not been established. Thus, the Examiner is respectfully requested to reconsider and withdraw this rejection.

VI. At page 17 of the Official Action, claims 1, 3, 5, 9 and 11 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Gavin et al. (WO 01/78738) in view of Calatayud et al

The Examiner asserts that Gavin et al. teaches medicinal compositions comprising (R,R)-formoterol and rofleponide as well as a propellant such as 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane or mixtures thereof.

In view of the following, this rejection is respectfully traversed.

A brief outline of relevant authority is set forth above in Section IV. Also, all references other than the Gavin et al. reference are discussed in detail in Section IV. For the sake of brevity, the discussion of the relevant authority and all references other than the Gavin et al. reference are incorporated herein in their entirety.

The Examiner relies on Gavin et al. for its alleged disclosure of formoterol with rofleponide, a corticosteroid. However, as discussed with respect to Aberg et al., Gavin et al. is absolutely silent regarding the presently claimed formulation comprising particles of formoterol and ciclesonide as described in the present

subject matter. Further, Gavin et al. does not even discuss ciclesonide, much less the synergistic benefits of a suspension comprising formoterol and ciclesonide. Thus, Gavin et al. does not contemplate the combination of formoterol and ciclesonide in a pharmaceutical suspension.

Therefore, the rejected claims are free of the prior art for the reasons discussed above (see, Section IV) and Applicants' arguments stated above are incorporated herein by reference in their entirety.

Accordingly, Applicants respectfully submit that a *prima facie* case of obviousness has not been established. Thus, the Examiner is respectfully requested to reconsider and withdraw this rejection.

VII. At page 19 of the Official Action, claims 2, 4 and 7-8 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Gavin et al. (WO 01/78738) in view of Calatayud et al. and further in view of Fassberg et al

The Examiner asserts that it would have been obvious to combine the teachings of Gavin and Fassberg because both references teach inhalable formulations comprising anti-inflammatory steroids that can be formulated as aerosol suspensions with hydrofluorocarbon propellants

In view of the following, this rejection is respectfully traversed.

A brief outline of relevant authority is set forth above in Section IV. Also, all cited references have been discussed in detail in previous sections. For the sake of brevity, the discussion of the relevant authority and all references are incorporated herein in their entirety.

The rejected claims are free of the prior art for the reasons discussed above (see, Section IV) and Applicants' arguments stated above are incorporated herein by reference in their entirety.

Accordingly, Applicants respectfully submit that a *prima facie* case of obviousness has not been established. Thus, the Examiner is respectfully requested to reconsider and withdraw this rejection.

VIII. At page 21 of the Official Action, claims 2, 4 and 7-8 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Gavin et al. (WO 01/78738) in view of Calatayud et al. and further in view of Keller et al. (WO 00/07567)

The Examiner asserts that Keller et al. teaches that the inclusion of solid salts of cromoglycic acid and/or nedocromil as a vehicle at non-therapeutically or non-prophylactically effective concentrations improves the dispersion characteristics and the chemical and physical stability or active ingredients which are sensitive to moisture and are present in pharmaceutical aerosol suspension formulations.

In view of the following, this rejection is respectfully traversed.

A brief outline of relevant authority is set forth above in Section IV. Also, all references other than the Keller et al. reference are discussed in detail in Section IV. For the sake of brevity, the discussion of the relevant authority and all references other than the Keller et al. reference are incorporated herein in their entirety.

The Examiner relies on Keller et al. for its alleged disclosure that the inclusion of disodium cromoglycate or nedocromil sodium to formulations can be used to stabilize moisture-sensitive compounds, such as formoterol fumarate as well as to reduce the tendency to adhesion of electrostatically charged active compounds, such as micronized corticosteroids.

However, the rejected claims are free of the prior art for the reasons discussed above (see, Section IV) and Applicants' arguments stated above are incorporated herein by reference in their entirety.

Accordingly, Applicants respectfully submit that a *prima facie* case of

obviousness has not been established. Thus, the Examiner is respectfully requested to reconsider and withdraw this rejection.

IX. At page 25 of the Official Action, claims 1 and 5 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 6 of copending U.S. Patent Application No. 10/537,356 in view of Burt and Aberg et al.

The Examiner asserts that independent claim 6 of the copending '356 application claims a formulation comprising R,R-formoterol and ciclesonide in a form administrable from a dry powder inhaler.

Applicants respectfully request that this rejection be held in abeyance until an indication that the claims are otherwise allowable. Applicants, at that time, will either address this rejection or file a terminal disclaimer.

CONCLUSION

In view of the foregoing, applicants submit that the presently pending claims are patentable over the cited references. Early notice to that effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

THE NATH LAW GROUP

January 12, 2010

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